DR. STEPHEN LAKE - CONFIDENTIAL

IN THE UNITED STATES DISTRICT COURT

FOR THE SOUTHERN DISTRICT OF NEW YORK

CIVIL ACTION NO.: 15 Civ. 08725 (GBD)

UMB BANK, N.A., AS TRUSTEES,)
)
Plaintiff,)
)
VS.)
)
SANOFI,)
)
Defendant.)

VIDEOTAPED DEPOSITION OF

DR. STEPHEN LAKE

CONFIDENTIAL - PURSUANT TO PROTECTIVE ORDER

BOSTON, MASSACHUSETTS

THURSDAY, NOVEMBER 16, 2017

REPORTED BY:
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Notary Public (CT, MA, RI)
CSR No. 000133

JOB NO.: 130190

disease, lysosomal storage disorder clinical trials.

And then at the end of 2006, I took on the responsibility as lead statistician for the Campath development program and was in that capacity throughout the -- the phase, pivotal design study and regulatory approval of Lemtrada.

In 2012, I took the position of head of Sanofi Genzyme biostatistics. So I was then responsible for the full portfolio underneath Sanofi Genzyme.

At the -- in March 2017, I left Sanofi and joined Clementia Pharmaceuticals, which is a small pharmaceutical company developing a drug for a very rare bone disease.

Q. And why did you leave Genzyme?

A. Well, I had been with Genzyme and then Sanofi for basically my entire career and decided I wanted a change. What I was doing in my -- at the time I left Sanofi I was an Associate Vice President of Biostatistics.

A. I think they were -- they were colleagues just discussing the CVR in general, and that was about it.

Q. Were those colleagues individuals who also worked on the Alemtuzumab team?

A. Yes.

Q. Do you recall any specific colleagues that you had those discussions with?

A. No.

Q. Did you have any discussions with any individuals who worked at Sanofi as opposed to Genzyme?

A. No.

Q. What was your role on the Alemtuzumab team?

A. So I was the lead biostatistician for the Alemtuzumab clinical development program. Then I also served as the -- the representative for a number of different functions at the -- at the clinical -- at the clinical development team level. So I represented biostatistics, programming, data management and medical writing.

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MR. AMSEL: As a general matter?

MR. LECOURS: Yes.

MR. AMSEL: Then objection to form. You can answer.

THE WITNESS: Randomized controlled clinical trials are done because what you would like to do is have the two groups that are being assessed in the treatment arms as similar as possible so that there's no underlying confounders that could bias the assessment of efficacy.

(BY MR. LECOURS):

Q. And the -- the controlled aspect of the study, what's -- what's the purpose of a control?

A. To provide a comparator for the therapy under study.

Q. Are there any other purposes?

A. Not that I can think of.

Q. What -- are you familiar with the concept of last patient/last value?

A. Yes.

Q. What -- and what generally does that concept mean?

the per protocol population analysis.

Q. So we -- we spoke previously about randomly controlled trials. Would you agree that one purpose to perform such a trial is to reduce bi- -- or reduce or remove bias?

A. A -- in terms of a randomized controlled study?

Q. Yes.

A. Yes.

Q. And what is bias just generally speaking in your understanding?

A. Bias -- well, the -- the technical definition would be that the expectation of the treatment effect in one group minus the expectation of the placebo response in the placebo group is not equal to the actual treatment difference.

It is impacted in some way by either the way the study was conducted or differences in the patient populations.

Q. And if there's no placebo group as with a rater-blinded study, how does -- how does bias -- how does bias arise in that

described earlier, to make sure the two groups are essentially equal statistically?

A. It is so that -- yes.

Q. So what's -- what's the purpose of using a placebo in a randomized controlled study?

A. A placebo as opposed to an active control?

Q. Yes.

A. So A placebo would be subject -- a placebo arm is something that the subject no -- receives no therapy other than the standard of care.

So if you're trying to establish that the efficacy of your treatment is better than receiving nothing but the standard of care, then you could conduct the placebo controlled study.

Q. Are you familiar with a double-dummy, double-blinded study?

A. Yes.

Q. And how -- how is that type of study designed?

A. Well, that would be when the -- a double-dummy -- sorry -- double-dummy, double blinded -- double-blinded study. So a double-dummy is when the -- you would have -- if you have a therapy under investigation, you have the therapy, and then you have a placebo version of that therapy.

And they are packaged such that you cannot distinguish between the two. And then the double-blind is when the -- the patient as well as the site staff administering the protocol are unaware of the treatment assignments.

Q. So in a double-dummy, double-blinded designed study, each treatment arm is getting an active -- an active comparator and a placebo; is that correct?

A. No. In a double-dummy study, a -- if it's a placebo-controlled study, one subject would be assigned the therapy under investigation if they were randomized to the investigational arm, and a -- another

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differently to clinical tests, particularly those tests in which they are subjective measures?

MR. AMSEL: Same objection. You can answer if you can.

THE WITNESS: I don't know. I -- I don't know.

(BY MR. LECOURS):

Q. So is it your view that there's no potential that bias could be introduced if patients, for example, in the Alemtuzumab study, knew what treatment arm they were on?

MR. AMSEL: Objection to the form.

THE WITNESS: I think -- I think bias could be introduced if subjects knew the treatment assignment. So...

(BY MR. LECOURS):

Q. And they did, right?

A. Right.

MR. AMSEL: They did what?

(BY MR. LECOURS):

Q. Know the treat -- what treatment

arm they were on --

A. Yes.

Q. -- right?

A. That was the design of the study.

[redacted]

Q. Okay. What's the statistical significance of having a -- of a baseline measure?

A. A baseline measure is what will be used to -- as the reference for change post-therapy and throughout the -- at the end of the study.

Q. So it's that which all future study -- future measurements are measured

Q. And that could be by using different medication choices with that patient, for example?

A. Yes.

[redacted]

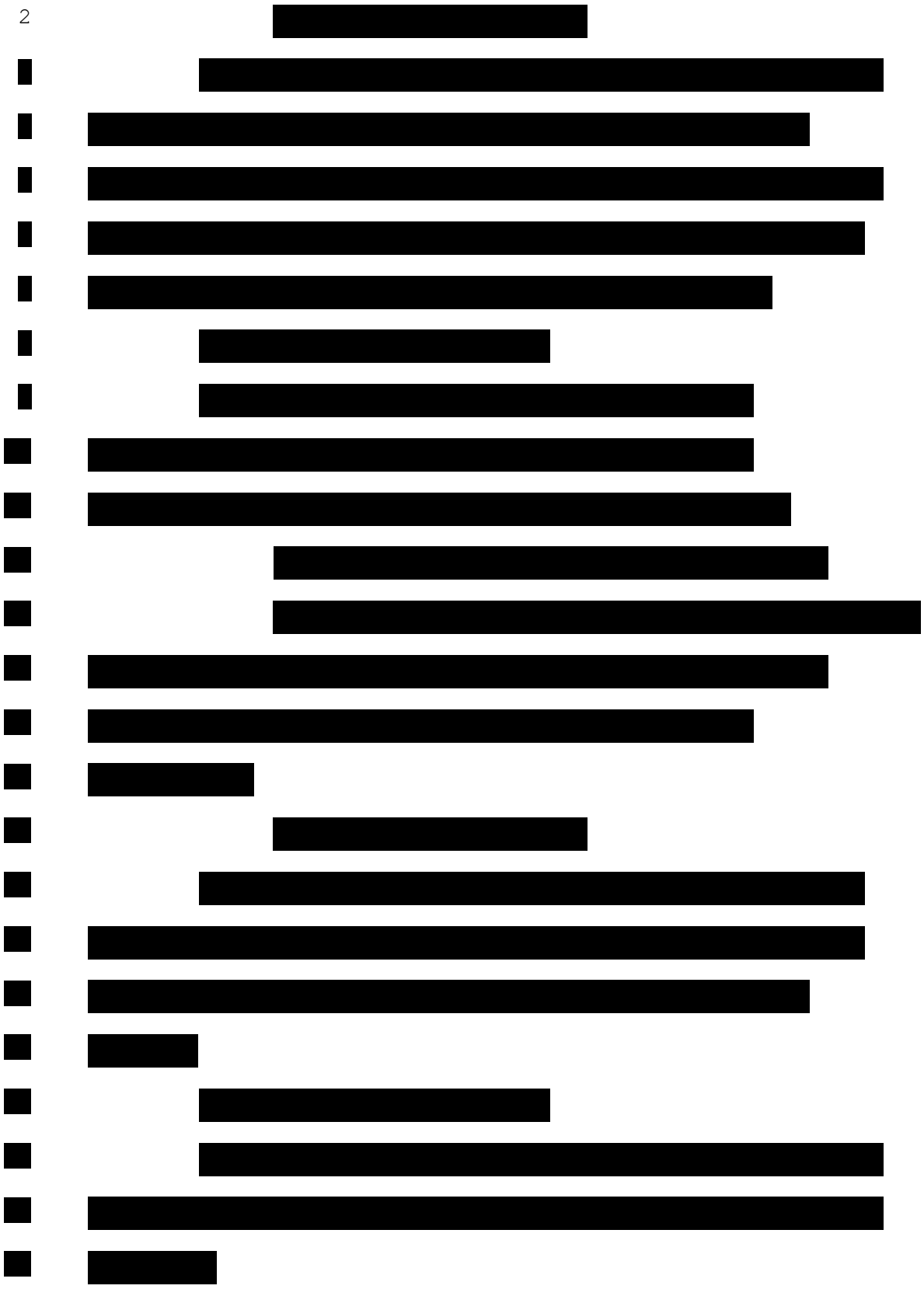
[redacted]

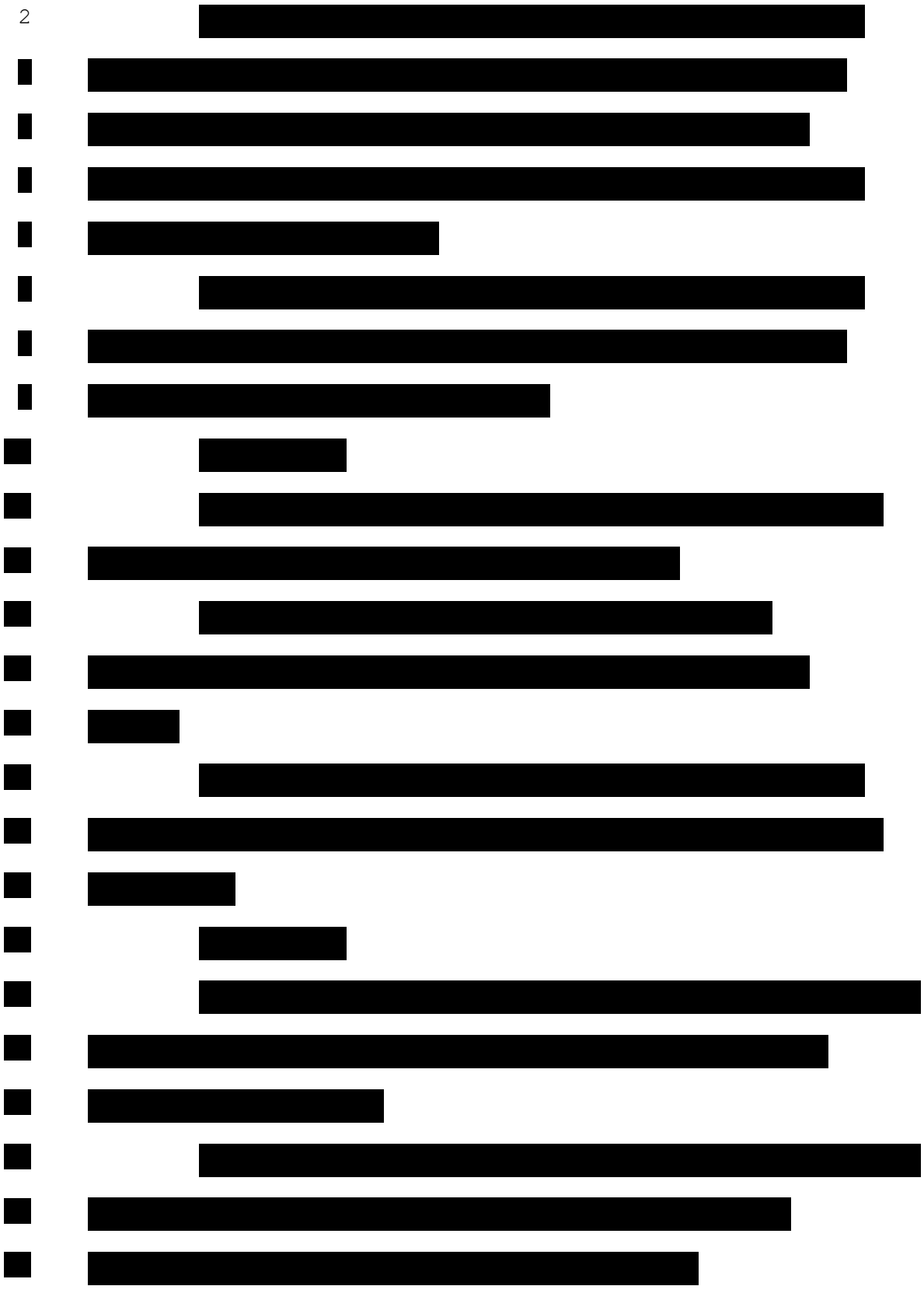
Q. And he -- he was the -- was he the -- he was the clinical reviewer at the FDA?

A. Medical reviewer.

Q. Medical reviewer. He wasn't the statistical reviewer?

A. No.





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[redacted]

(BY MR. LECOURS):

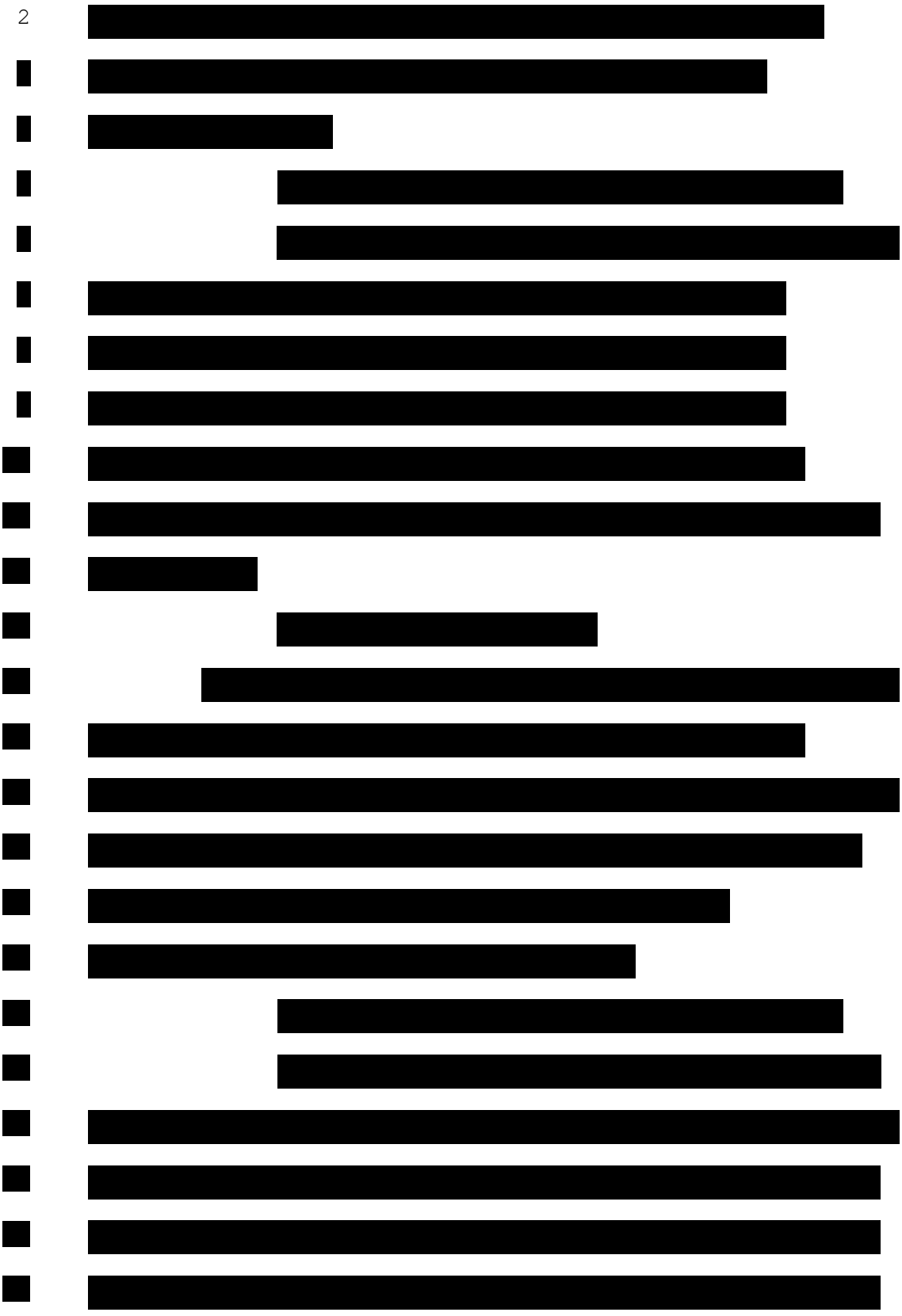
Q. I'm going to hand you what's been previously marked as Plaintiff's 32.

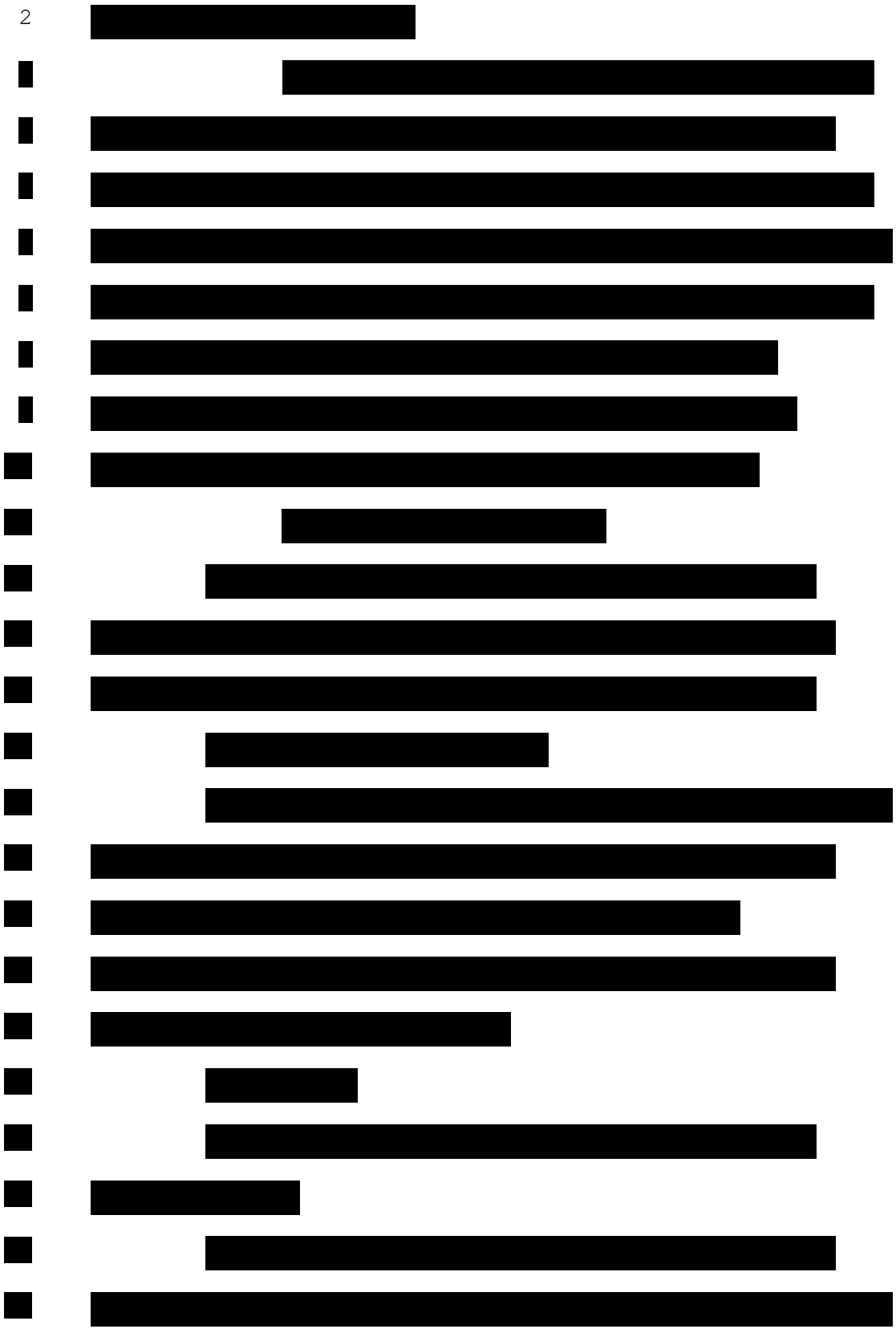
(Whereupon, Exhibit No. 32, Letter, previously marked, was referenced)

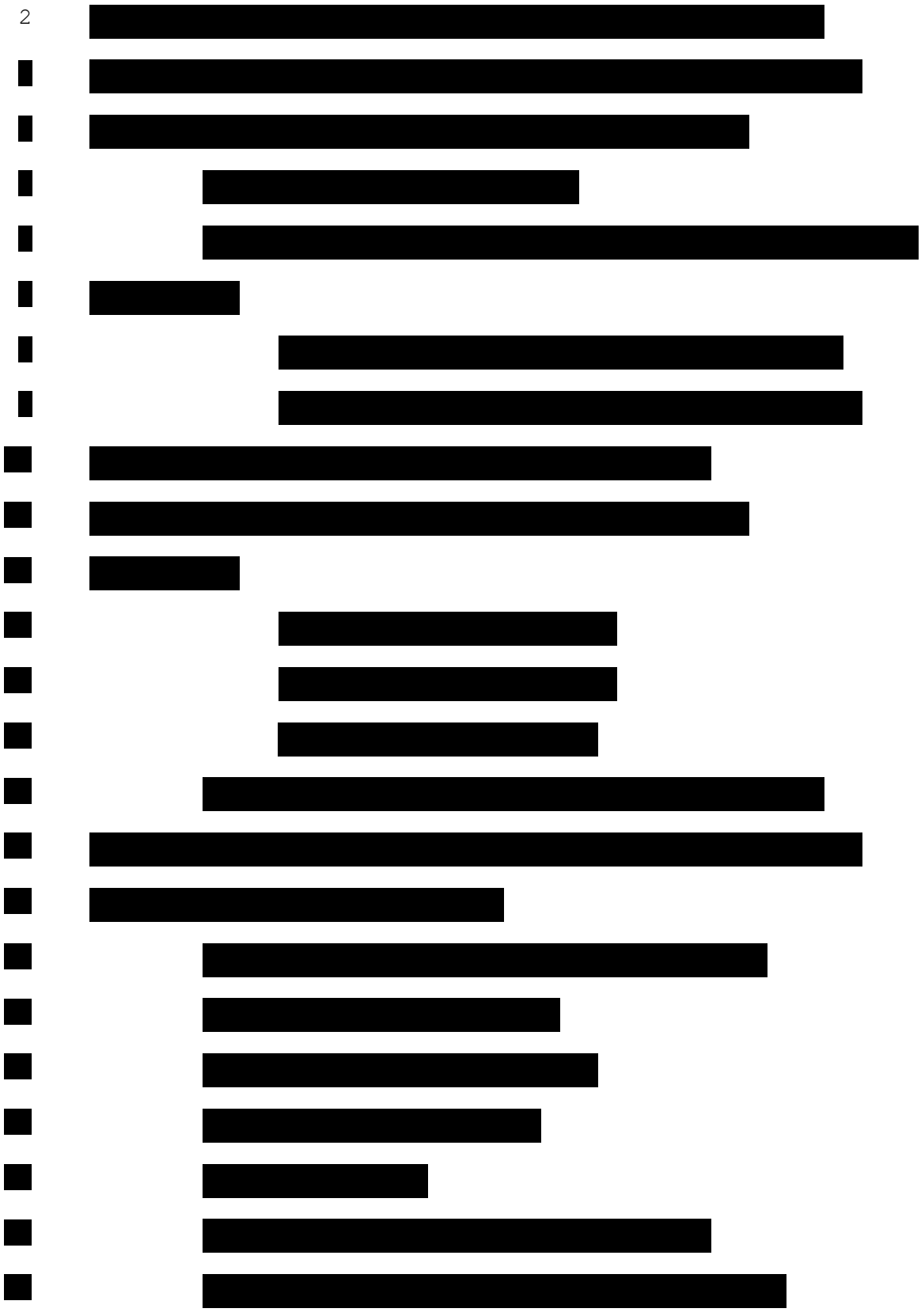
(BY MR. LECOURS):

Q. Are you familiar with this

[redacted]







[redacted]

Q. And the article we looked at, the -- the one that's -- I believe it's a document, Plaintiff's 90. It's titled "Alemtuzumab improves preexisting disability in active, relapse and remitting MS patients."

What data was this article based on?

A. The CARE-MS 324 study.

Q. And if you turn all the way to the end of the article, the last text before "Alter-Contributions" states, "The outcomes presented here not only support Alemtuzumab's ability to slow disability accumulation, but also demonstrate superior benefit in improving preexisting disability in patients with RRMS with an inadequate response to prior DMT."

Do you agree with that statement?

A. Yes.

Q. Yeah, you can set that article to